

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 18 August 2011 has been entered.

Status of the Claims

2. Claims 47, 49, 59 and 61 have been cancelled; Claims 41 and 46, 48, 50-58, 60, 62-70 are pending and subject to examination on the merits.

Withdrawal of Previous Objections/Rejections

3. The rejection of claims 41, 46 and 70 (and their dependent claims 48-58 and 60-69) under 35 USC 112 2nd paragraph is withdrawn in view of the amendments to the claims.

4. The rejection of claims 49 and 61 under 35 USC 112 4th paragraph is moot in view of the cancellation of said claims. The rejection of claim 55 under the same statute is withdrawn in view of the amendment to the claim to recite 97% identity and thus further limit the parent claim.

5. The rejection of claims 41, 46-49, 51, 52, 59-61, 63, 64 and 66-69 under 35 U.S.C. 102(b) as anticipated by Hartford and Dowds (Microbiology, 1994, Vol. 140, pp. 297-304) as evidenced by Chen et al. (Mol. Micro., 1995, cited on IDS) and by Naclerio et al. (App. Env. Micro., 1995, 61(12):4471-4473) is withdrawn in view of the amendments to the claims. Specifically, Hartford and Dowds teach the over production of endogenous proteins of interest and that the MrgA is also endogenous and/or is not operatively linked to a heterologous promoter.

New Objections/Rejections – Necessitated by Amendments

Claim Objections

6. Claims 46 and 70 recite two part (a)'s and two part (b)'s which make the claim less clear than is necessary. As such, said claims are objected to for said informalities. Appropriate correction is required.

Maintained/Modified Rejections

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 41, 46, 48, 50-58, 60, 62-70 are rejected under 35 U.S.C. 102(b) as being anticipated by Chen et al. (1995, PNAS, Vol. 140, pp. 297-304).

Chen et al. teach the creation of various strains of *Bacillus subtilis* which have been transformed with exogenous chromosomal *mrgA-lacZ* fusion DNA which is then fused to either the *mrgA* or *katA* promoters and expressed (see p. 8190 and p. 8192, as recited below). Said expression results in progeny cells which produce greater amounts of the fusion construct than the parent strain. It is specifically taught:

Each cured strain (HB13XX series) suspected of carrying a trans-acting mutation (because the constitutive phenotype was not phage-linked) was transduced to resistance to erythromycin and colinomycin by SPβ1122, generating strains HB12XXB, and constitutive expression of β-gal was confirmed. To study the regulation of *mrgA* and *mrgC* (1) in these mutant backgrounds, each HB13XX strain was transformed with HB1022(*mrgA-lacZ*)chromosomal DNA (1), generating strains HB14XX, or was transduced with SPβ085(*mrgC-cat-lacZ*), generating strains HB15XX. – See p. 8190, 2nd col., last paragraph.

And (see p. 8192, 1st col., 2nd and 3rd paragraphs):

Characterization of Trans-Acting Mutations. To define factors involved in the regulation of *mrgA*, we have characterized 12 trans-acting mutants. Each mutant was cured of the SPβ1122 prophage, and transcriptional fusions to the *mrgA* (HB14XX series) and *mrgC* (HB15XX series) promoters were introduced. All 12 HB14XX strains displayed increased *mrgA-lacZ* expression, which was repressed little, if at all, by addition of Mn(II) (data not shown). We have described a second metalloregulated gene in *B. subtilis*, *mrgC*, which is repressed by iron but not by Mn(II) (1). In all 12 HB15XX strains, both *mrgC-lacZ* expression and the synthesis of catecholate siderophores were repressed normally by iron (data not shown). Therefore, regulation of *mrgA* expression [by both Mn(II) and iron] is independent of the postulated iron-dependent repressor, which regulates siderophore biosynthesis and *mrgC* expression.

Like our trans-acting mutants, an H202R strain isolated previously, MA991 (8), is derepressed for *mrgA* expression. MA991 has a characteristic protein profile when analyzed by Coomassie-stained SDS/PAGE: *MrgA*, *KatA*, *AhpC*, and *AhpF* are all overproduced (8, 42). Nine of our trans-acting mutants shared this altered protein profile (data not shown) and are therefore likely to be mutant in the same regulatory pathway or even the same gene.

Therefore, the protein of interest can be the β -galactosidase, e.g. a heterologous exoprotein and the MrgA protein is operatively fused to either the MrgA promoter OR the heterologous KatA promoter.

Applicants Remarks and Examiner's Rebuttal:

Applicants state that they believe the amended claims overcome the rejection of by Chen et al. but provide no rationale or reasoning in making these assertions.

The MrgA protein fused to LacZ are clearly overexpressed, said construct and said LacZ are furthermore heterologous. Since said LacZ is identified/construed as a protein of interest, the MrgA-LacZ construct is further operatively linked to the heterologous promoter KatA, the limitations of the claims have been met.

Conclusion

9. No claim is allowed.
10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUZANNE M. NOAKES whose telephone number is (571)272-2924. The examiner can normally be reached on 7.00 AM-3.00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath Rao can be reached on 571-272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/SUZANNE M. NOAKES/
Primary Examiner, Art Unit 1656
26 August 2011